

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1. (Currently amended) An oxidation resistant engineered ribonuclease inhibitor variant ~~for~~ of a ribonuclease inhibitor which natively has adjacent cysteine residues, the variant differing in amino acid sequence from the native form of the ribonuclease inhibitor only by having at least one amino acid substitution in at least one of two adjacent cysteine residues present in the amino acid sequence of the wild-type ribonuclease inhibitor, the substitution ~~being to~~ for the cysteine residue being an amino acid residue not capable of forming a disulfide bond with an adjacent residue, the substituted ribonuclease inhibitor variant having a greater resistance to oxidation, the substituted ribonuclease inhibitor variant retaining its specificity and binding affinity to ribonuclease.

2. (Previously presented) The ribonuclease inhibitor of claim 1, wherein ribonuclease inhibitor is a human ribonuclease inhibitor and the substituted cysteine residue is in at least one of positions 95, 96, 329 and 330.

3. (Original) The ribonuclease inhibitor of claim 1, wherein the cysteine residue is replaced with an alanine residue.

4. (Original) The ribonuclease inhibitor of claim 1, wherein the substitution in at least one of the cysteine residues inhibits the formation of a disulfide bond with an adjacent cysteine residue.

5. (Original) The ribonuclease inhibitor of claim 1, wherein the mutant ribonuclease inhibitor is 10 to 15 fold more resistant to oxidative damage than the native human ribonuclease inhibitor.

6. (Original) The ribonuclease inhibitor of claim 1, wherein the ribonuclease is of the RNASE A superfamily.

7. (Original) The ribonuclease inhibitor of claim 1, wherein the modified ribonuclease inhibitor exhibits an in vitro inhibition of ribonucleolytic activity.

8. Cancelled.

9. (Currently amended) A human ribonuclease inhibitor variant having at least one amino acid substitution in at least one of two adjacent cysteine residues present in the amino acid sequence of the wild-type ribonuclease inhibitor, the substitution being an amino acid other than cysteine, the remainder of the variant having the amino acid sequence of the wild-type ribonuclease inhibitor, the substituted ribonuclease inhibitor having a greater resistance to oxidation, the substituted ribonuclease inhibitor retaining the specificity and binding affinity to angiogenin of the wild-type human ribonuclease inhibitor.

10. (Previously presented) The ribonuclease inhibitor of claim 9, wherein the substituted cysteine residue is in at least one of positions 95, 96, 329, and 330.

11. to 14. Cancelled

15. (Currently amended) A human ribonuclease inhibitor variant ~~having comprising a protein having the amino acid sequence of native human ribonuclease inhibitor except for an~~ at least one amino acid substitution in at least ~~one~~ two of the amino acids positions 95, 96, 329, and 330 of the native human ribonuclease inhibitor, ~~the each~~ substitution being an alanine for a cysteine, the substituted ribonuclease inhibitor having a greater resistance to oxidation as compared to the wild-type human ribonuclease inhibitor, the substituted ribonuclease inhibitor retaining the specificity and binding affinity to angiogenin of the wild-type human ribonuclease inhibitor.

Application No.: 09/234,028
Response dated: July 19, 2006
Reply to Final Office Action dated: January 19, 2006

16. (New) A human ribonuclease inhibitor variant comprising a protein having the amino acid sequence of SEQ ID NO:3.